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L3 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1
AN 2006144978 MEDLINE
DN PubMed ID: 16516852
TI Interaction of bHLH-PAS proteins involved in juvenile hormone reception in
Drosophila.
AU Godlewski Jakub; Wang Shaoli; Wilson Thomas G
CS Department of Entomology, 400 Aronoff Laboratory, Ohio State University,
Columbus, OH 43210, USA.
NC AI052290 (NIAID)
SO Biochemical and biophysical research communications, (2006 Apr 21) Vol.
342, No. 4, pp. 1305-11. Electronic Publication: 2006-02-28.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200605
ED Entered STN: 15 Mar 2006
Last Updated on STN: 5 May 2006
Entered Medline: 4 May 2006
AB The Methoprene-tolerant (Met) bHLH-PAS gene is involved in juvenile
hormone (JH) action in Drosophila melanogaster as a likely component of a
JH receptor. We expressed Met in Drosophila S2 cells and explored for MET
partners using pull-down assays. MET-MET interaction was found to occur.
The germ-cell expressed (gce) gene is another D. melanogaster bHLH-PAS
gene with high homology to Met, and GCE formed heterodimers with MET. In
the presence of JH or either of two JH agonists, MET-MET and MET-GCE
formation was drastically reduced. Interaction between GCE and MET having
N- or C-terminus truncations, bHLH or PAS-A domain deletions, or a point
mutation in the PAS-B domain failed to occur.
However, JH-dependent interaction occurred between GCE and MET having
point mutations in bHLH or PAS-A. During development, changes in JH titer
may alter partner binding by MET and result in different gene expression
patterns.

L3 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 2
AN 2005432480 MEDLINE
DN PubMed ID: 16098197
TI Spectroscopic characterization of the isolated heme-bound PAS-B domain of
neuronal PAS domain protein 2 associated with circadian rhythms.
AU Koudo Ryoji; Kurokawa Hirofumi; Sato Emiko; Igarashi Jotaro; Uchida
Takeshi; Sagami Ikuko; Kitagawa Teizo; Shimizu Toru
CS Institute of Multidisciplinary Research for Advanced Materials, Tohoku
University, Sendai, Japan.
SO The FEBS journal, (2005 Aug) Vol. 272, No. 16, pp. 4153-62.
Journal code: 101229646. ISSN: 1742-464X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 16 Aug 2005
Last Updated on STN: 1 Oct 2005
Entered Medline: 30 Sep 2005
AB Neuronal PAS domain protein 2 (NPAS2) is an important transcription factor
associated with circadian rhythms. This protein forms a heterodimer with
BMAL1, which binds to the E-box sequence to mediate circadian
rhythm-regulated transcription. NPAS2 has two PAS domains with
heme-binding sites in the N-terminal portion. In this study, we
overexpressed wild-type and His mutants of the PAS-
B domain (residues 241-416) of mouse NPAS2 and then purified and
characterized the isolated heme-bound proteins. Optical absorption
spectra of the wild-type protein showed that the Fe(III), Fe(II) and
Fe(II)-CO complexes are 6-co-ordinated low-spin complexes. On the other
hand, resonance Raman spectra indicated that both the Fe(III) and Fe(II)
complexes contain mixtures of 5-co-ordinated high-spin and 6-co-ordinated
low-spin complexes. Based on inverse correlation between nu(Fe-CO) and
nu(C-O) of the resonance Raman spectra, it appeared that the axial ligand
trans to CO of the heme-bound PAS-B is His. Six His mutants (His266Ala,
His289Ala, His300Ala, His302Ala, His329Ala, and His335Ala) were generated,
and their optical absorption spectra were compared. The spectrum of the

His335Ala mutant indicated that its Fe(III) complex is the 5-co-ordinated high-spin complex, whereas, like the wild-type, the complexes for the five other His mutants were 6-co-ordinated low-spin complexes. Thus, our results suggest that one of the axial ligands of Fe(III) in PAS-B is His335. Also, binding kinetics suggest that heme binding to the PAS-B domain of NPAS2 is relatively weak compared with that of sperm whale myoglobin.

L3 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 3
AN 2003605708 MEDLINE
DN PubMed ID: 14551206
TI Relationships between heme incorporation, tetramer formation, and catalysis of a heme-regulated phosphodiesterase from Escherichia coli: a study of deletion and site-directed mutants.
AU Yoshimura Tokiko; Sagami Ikuko; Sasakura Yukie; Shimizu Toru
CS Institute of Multidisciplinary Research for Advanced Materials, Tohoku University, Sendai 980-8577, Japan.
SO The Journal of biological chemistry, (2003 Dec 26) Vol. 278, No. 52, pp. 53105-11. Electronic Publication: 2003-10-09.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200402
ED Entered STN: 23 Dec 2003
Last Updated on STN: 11 Feb 2004
Entered Medline: 10 Feb 2004
AB The heme-regulated phosphodiesterase (PDE) from Escherichia coli (Ec DOS) is a tetrameric protein composed of an N-terminal sensor domain (amino acids 1-201) containing two PAS domains (PAS-A, amino acids 21-84, and PAS-B, amino acids 144-201) and a C-terminal catalytic domain (amino acids 336-799). Heme is bound to the PAS-A domain, and the redox state of the heme iron regulates PDE activity. In our experiments, a H77A mutation and deletion of the PAS-B domain resulted in the loss of heme binding affinity to PAS-A. However, both

mutant proteins were still tetrameric and more active than the full-length wild-type enzyme (140% activity compared with full-length wild type), suggesting that heme binding is not essential for catalysis. An N-terminal truncated mutant (DeltaN147, amino acids 148-807) containing no PAS-A domain or heme displayed 160% activity compared with full-length wild-type protein, confirming that the heme-bound PAS-A domain is not required for catalytic activity. An analysis of C-terminal truncated mutants led to mapping of the regions responsible for tetramer formation and revealed PDE activity in tetrameric proteins only. Mutations at a putative metal-ion binding site (His-590, His-594) totally abolished PDE activity, suggesting that binding of Mg2+ to the site is essential for catalysis. Interestingly, the addition of the isolated PAS-A domain in the Fe2+ form to the full-length wild-type protein markedly enhanced PDE activity (>5-fold). This activation is probably because of structural changes in the catalytic site as a result of interactions between the isolated PAS-A domain and that of the holoenzyme.

L3 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:230819 BIOSIS
DN PREV200300230819
TI Thymocyte alterations in CD2-driven constitutively active arylhydrocarbon receptor (AhR) transgenic mice.
AU Nohara, K. [Reprint Author]; Tsukumo, S. [Reprint Author]; Ito, T. [Reprint Author]; Yamamoto, M.; Motohashi, H.; Hida, A.; Fujii-Kuriyama, Y.; Inouye, K. [Reprint Author]; Nagai, H. [Reprint Author]; Tohyama, C. [Reprint Author]
CS Environmental Health Sciences Division, National Institute for Environmental Studies, Tsukuba, Japan
SO Toxicological Sciences, (March 2003) Vol. 72, No. S-1, pp. 362. print.
Meeting Info.: 42nd Annual Meeting of the Society of Toxicology. Salt Lake

City, Utah, USA. March 09-13, 2003. Society of Toxicology.
ISSN: 1096-6080 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 May 2003
Last Updated on STN: 14 May 2003

L3 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 4
AN 2001664334 MEDLINE
DN PubMed ID: 11551926
TI Definition of a dioxin receptor mutant that is a constitutive activator of
transcription: delineation of overlapping repression and ligand binding
functions within the PAS domain.
AU McGuire J; Okamoto K; Whitelaw M L; Tanaka H; Poellinger L
CS Department of Cell and Molecular Biology, Medical Nobel Institute,
Karolinska Institute, S-171 77 Stockholm, Sweden.
SO The Journal of biological chemistry, (2001 Nov 9) Vol. 276, No. 45, pp.
41841-9. Electronic Publication: 2001-09-10.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 19 Nov 2001
Last Updated on STN: 5 Jan 2003
Entered Medline: 5 Dec 2001
AB The intracellular dioxin (aryl hydrocarbon) receptor is a ligand-activated
transcription factor that mediates the adaptive and toxic responses to
environmental pollutants such as
2,3,7,8-tetrachlorodibenzo-p-dioxin and
structurally related congeners. Whereas the ligand-free receptor is
characterized by its association with the molecular chaperone hsp90,
exposure to ligand initiates a multistep activation process involving
nuclear translocation, dissociation from the hsp90 complex, and
dimerization with its partner protein Arnt. In this study, we have
characterized a dioxin receptor deletion mutant lacking the minimal
ligand-binding domain of the receptor. This mutant did not bind ligand

and localized constitutively to the nucleus. However, this protein was functionally inert since it failed to dimerize with Arnt and to bind DNA. In contrast, a dioxin receptor deletion mutant lacking the minimal PAS B motif but maintaining the N-terminal half of the ligand-binding domain showed constitutive dimerization with Arnt, bound DNA, and activated transcription in a ligand-independent manner. Interestingly, this mutant showed a more potent functional activity than the dioxin-activated wild-type receptor in several different cell lines. In conclusion, the constitutively active dioxin receptor may provide an important mechanistic tool to investigate receptor-mediated regulatory pathways in closer detail.

L3 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 5
AN 94344118 MEDLINE
DN PubMed ID: 8065341
TI Identification of functional domains of the aryl hydrocarbon receptor nuclear translocator protein (ARNT).
AU Reisz-Porszasz S; Probst M R; Fukunaga B N; Hankinson O
CS Laboratory of Structural Biology and Molecular Medicine, University of California, Los Angeles 90024-1786.
NC NCI CA16042 (NCI)
NCI CA28868 (NCI)
SO Molecular and cellular biology, (1994 Sep) Vol. 14, No. 9, pp. 6075-86.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U10325
EM 199409
ED Entered STN: 5 Oct 1994
Last Updated on STN: 5 Oct 1994
Entered Medline: 19 Sep 1994
AB The activated aryl hydrocarbon receptor (AHR) and the AHR nuclear translocator (ARNT) bind DNA as a heterodimer. Both proteins represent a novel class of basic helix-loop-helix (bHLH)-containing transcription factors in that (i) activation of AHR requires the binding of ligand

(e.g., 2,3,7,8-tetrachlorodibenzo-p-dioxin [TCDD]), (ii) the xenobiotic responsive element (XRE) recognized by the AHR/ARNT heterodimer differs from the recognition sequence for nearly all other bHLH proteins, and (iii) both proteins contain a PAS homology region, which in the Drosophila PER and SIM proteins functions as a dimerization domain. A cDNA for mouse ARNT has been cloned, and potential functional domains of ARNT were investigated by deletion analysis. A mutant lacking all regions of ARNT other than the bHLH and PAS regions is unimpaired in TCDD-dependent dimerization and subsequent XRE binding and only modestly reduced in ability to complement an ARNT-deficient mutant cell line, c4, in vivo. Both the first and second alpha helices of the bHLH region are required for dimerization. The basic region is required for XRE binding but not for dimerization. Deletion of either the A or B segments of the PAS region slightly affects TCDD-induced heterodimerization, while deletion of the complete PAS region severely affects (but does not eliminate) dimerization. Thus, ARNT possesses multiple domains required for maximal heterodimerization. Mutants deleted for PAS A, PAS B, and the complete PAS region all retain some degree of XRE binding, yet none can rescue the c4 mutant. Therefore, both the PAS A and PAS B segments, besides contributing to dimerization, apparently fulfill additional, unknown functions required for biological activity of ARNT.

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Interaction of bHLH-PAS proteins involved in juvenile hormone reception in Drosophila.
Biochem Biophys Res Commun. 2006 Apr 21;342(4):1305-11. Epub 2006 Feb 28.
PMID: 16516852 [PubMed - indexed for MEDLINE]

2: Yang J, Zhang L, Erbel PJ, Gardner KH, Ding K, Garcia JA, Bruick RK. Related Articles, Links

Functions of the Per/ARNT/Sim domains of the hypoxia-inducible factor.
J Biol Chem. 2005 Oct 28;280(43):36047-54. Epub 2005 Aug 29.
PMID: 16129688 [PubMed - indexed for MEDLINE]

3: Uchida T, Sato E, Sato A, Sagami I, Shimizu T, Kitagawa T. Related Articles, Links

CO-dependent activity-controlling mechanism of heme-containing CO-sensor protein, neuronal PAS domain protein 2.
J Biol Chem. 2005 Jun 3;280(22):21358-68. Epub 2005 Mar 29.
PMID: 15797872 [PubMed - indexed for MEDLINE]

4: Yildiz O, Doi M, Yujnovsky I, Cardone L, Berndt A, Hennig S, Schulze S, Urbanke C, Sassone-Corsi P, Wolf E. Related Articles, Links

Crystal structure and interactions of the PAS repeat region of the Drosophila clock protein PERIOD.
Mol Cell. 2005 Jan 7;17(1):69-82.
PMID: 15629718 [PubMed - indexed for MEDLINE]

5: Katschinski DM, Le L, Schindler SG, Thomas T, Voss AK, Wenger RH. Related Articles, Links

Interaction of the PAS B domain with HSP90 accelerates hypoxia-inducible factor-1alpha stabilization.
Cell Physiol Biochem. 2004;14(4-6):351-60.
PMID: 15319539 [PubMed - indexed for MEDLINE]

6: Yoshimura T, Sagami I, Sasakura Y, Shimizu T. Related Articles, Links

Relationships between heme incorporation, tetramer formation, and catalysis of a heme-regulated phosphodiesterase from Escherichia coli: a study of deletion and site-

directed mutants.
J Biol Chem. 2003 Dec 26;278(52):53105-11. Epub 2003 Oct 9.
PMID: 14551206 [PubMed - indexed for MEDLINE]

☐ **7:** McGuire J, Okamoto K, Whitelaw ML, Tanaka H, Poellinger L. Related Articles, Links

Definition of a dioxin receptor mutant that is a constitutive activator of transcription: delineation of overlapping repression and ligand binding functions within the PAS domain.
J Biol Chem. 2001 Nov 9;276(45):41841-9. Epub 2001 Sep 10.
PMID: 11551926 [PubMed - indexed for MEDLINE]

☐ **8:** Wang L, Fabret C, Kanamaru K, Stephenson K, Dartois V, Perego M, Hoch JA. Related Articles, Links

Dissection of the functional and structural domains of phosphorelay histidine kinase A of Bacillus subtilis.
J Bacteriol. 2001 May;183(9):2795-802.
PMID: 11292798 [PubMed - indexed for MEDLINE]

☐ **9:** Kronenberg S, Esser C, Carlberg C. Related Articles, Links

An aryl hydrocarbon receptor conformation acts as the functional core of nuclear dioxin signaling.
Nucleic Acids Res. 2000 Jun 15;28(12):2286-91.
PMID: 10871357 [PubMed - indexed for MEDLINE]

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Characterization of three splice variants and genomic organization of the mouse BMAL1 gene.
Biochem Biophys Res Commun. 1999 Jul 14;260(3):760-7.
PMID: 10403839 [PubMed - indexed for MEDLINE]

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A mutation in the aryl hydrocarbon receptor (AHR) in a cultured mammalian cell line identifies a novel region of AHR that affects DNA binding.
J Biol Chem. 1997 Dec 12;272(50):31845-54.
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☐ **12:** Numayama-Tsuruta K, Kobayashi A, Sogawa K, Fujii-Kuriyama Y. Related Articles, Links

A point mutation responsible for defective function of the aryl-hydrocarbon-receptor nuclear translocator in mutant Hepa-1c1c7 cells.
Eur J Biochem. 1997 Jun 1;246(2):486-95.
PMID: 9208942 [PubMed - indexed for MEDLINE]

☐ **13:** Fukunaga BN, Probst MR, Reisz-Porszasz S, Hankinson O. Related Articles, Links

Identification of functional domains of the aryl hydrocarbon receptor.
J Biol Chem. 1995 Dec 8;270(49):29270-8.
PMID: 7493958 [PubMed - indexed for MEDLINE]

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PMID: 16181639 [PubMed - indexed for MEDLINE]

2: Yang J, Zhang L, Erbel PJ, Gardner KH, Ding K, Garcia JA, Bruick RK. Related Articles, Links

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J Biol Chem. 2005 Oct 28;280(43):36047-54. Epub 2005 Aug 29.
PMID: 16129688 [PubMed - indexed for MEDLINE]

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J Biol Chem. 2005 Jun 3;280(22):21358-68. Epub 2005 Mar 29.
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PMID: 15629718 [PubMed - indexed for MEDLINE]

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Cell Physiol Biochem. 2004;14(4-6):351-60.
PMID: 15319539 [PubMed - indexed for MEDLINE]

6: Korkalainen M, Tuomisto J, Pohjanvirta R. Related Articles, Links

Primary structure and inducibility by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) of aryl hydrocarbon receptor repressor in a TCDD-sensitive and a TCDD-resistant rat

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Acta Crystallogr D Biol Crystallogr. 2004 Mar;60(Pt 3):550-2. Epub 2004 Feb 25.
PMID: 14993689 [PubMed - indexed for MEDLINE]

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Structure of the NCoA-1/SRC-1 PAS-B domain bound to the LXXLL motif of the STAT6 transactivation domain.
J Mol Biol. 2004 Feb 13;336(2):319-29.
PMID: 14757047 [PubMed - indexed for MEDLINE]

☐ **9:** Erbel PJ, Card PB, Karakuzu O, Bruick RK, Gardner KH. Related Articles, Links

Structural basis for PAS domain heterodimerization in the basic helix--loop--helix-PAS transcription factor hypoxia-inducible factor.
Proc Natl Acad Sci U S A. 2003 Dec 23;100(26):15504-9. Epub 2003 Dec 10.
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Relationships between heme incorporation, tetramer formation, and catalysis of a heme-regulated phosphodiesterase from Escherichia coli: a study of deletion and site-directed mutants.
J Biol Chem. 2003 Dec 26;278(52):53105-11. Epub 2003 Oct 9.
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Dissection of the functional and structural domains of phosphorelay histidine kinase A of Bacillus subtilis.
J Bacteriol. 2001 May;183(9):2795-802.
PMID: 11292798 [PubMed - indexed for MEDLINE]

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